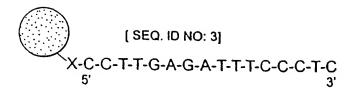
WO 02/18643

1/64

PCT/US01/25237

FIG. 1



G-G-A-A-C-T-C-T-A-A-A-G-G-G-A-G-X
[SEQ. ID NO: 4]



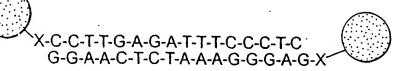


FIG. 2

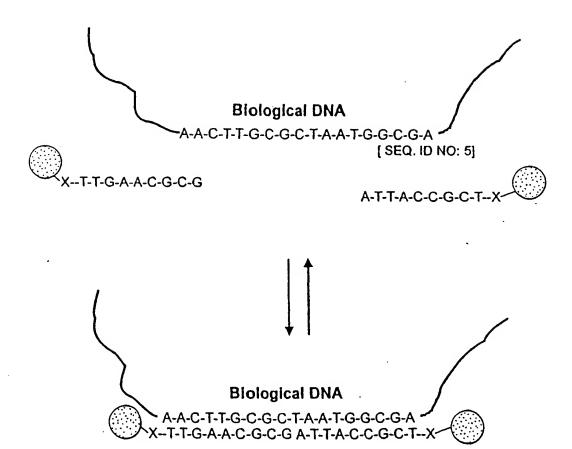
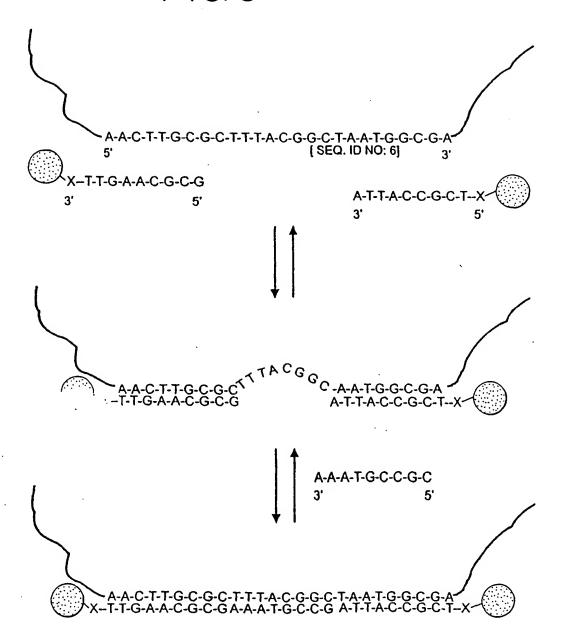
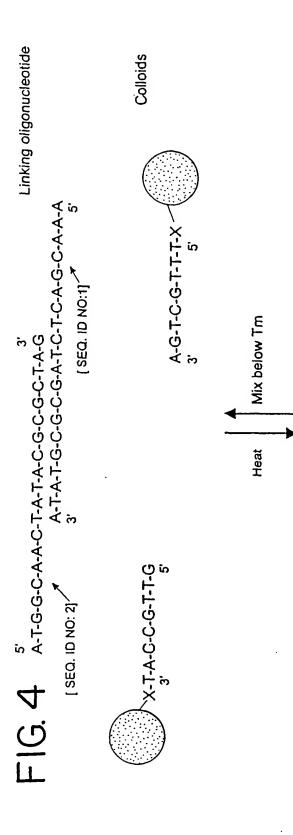


FIG. 3





Stand below Tm A-T-G-G-C-A-A-C-T-A-T-A-C-G-C-G-C-T-A-G A-G-X-T-A-C-C-G-T-T-G A-T-A-T-G-C-G-C-G-A-T-C-Heat

Precipitate (formed by further cross-linking)

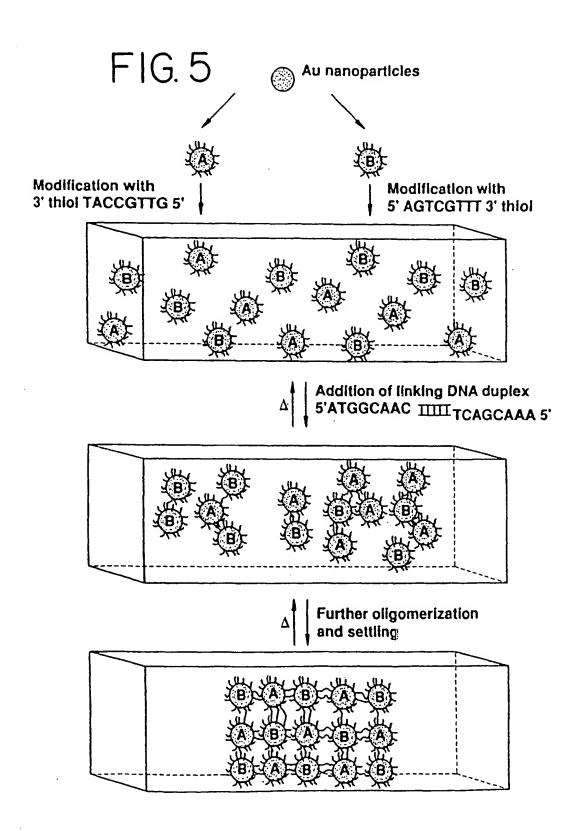
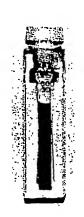
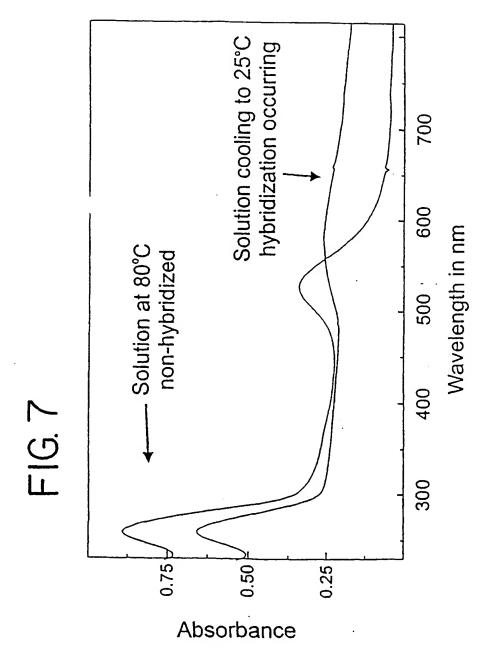


FIG.6A FIG.6B FIG.6C









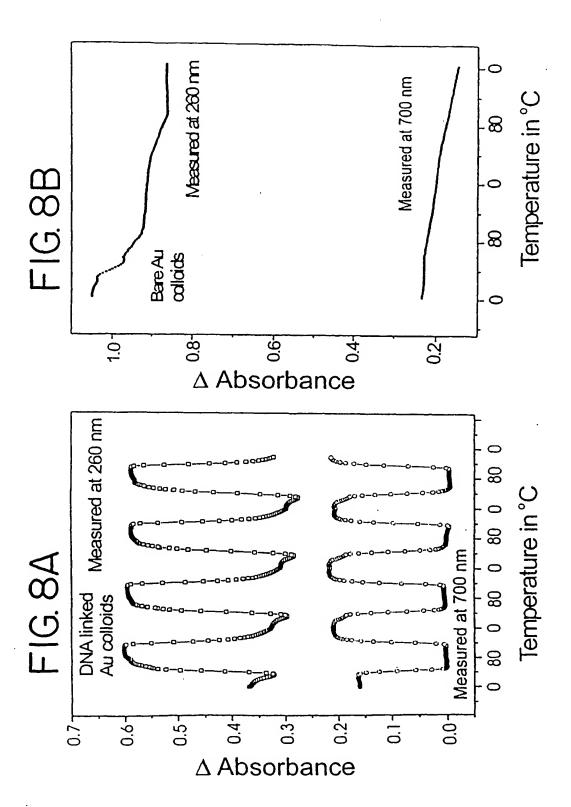


FIG. 9A

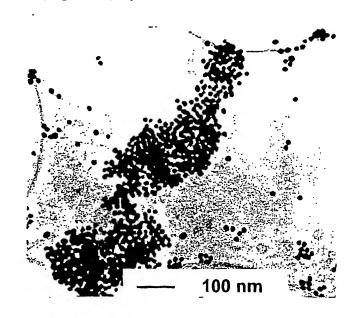
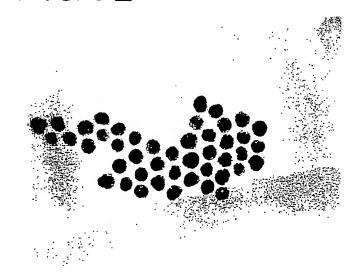
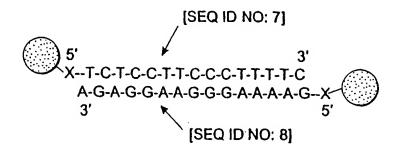


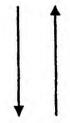
FIG.9B

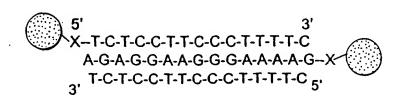


— 33 nm



3' T-C-T-C-C-T-T-C-C-C-T-T-T-T-C 5' [SEQ ID NO: 9]





F1G. __

[SEC D NO: 10]
S-A-T-G-G-C-A-A-C-T-A-T-A-C-G-C-G-C-I-A-G-A-G-T-C-G-T-T-T
5'
3'

T-A-C-C-G-T-T-G-A-T-A-T-G-C-G-C-G-A-T-C-T-C-A-G-C-A-A--S-3' [SEQ. ID NO: 11]

•

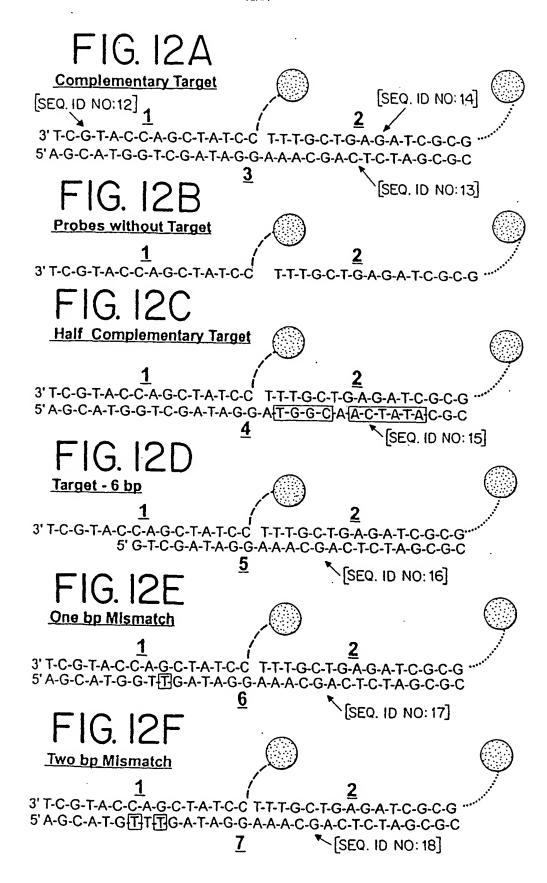
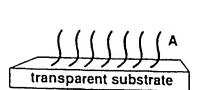


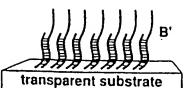
FIG. 13A



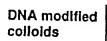
Modified DNA chemisorbed onto solld substrate



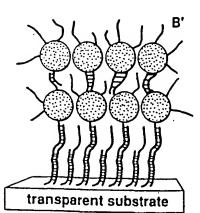
Analyte DNA



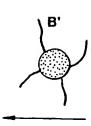
Analyte DNA hybridized onto substrate

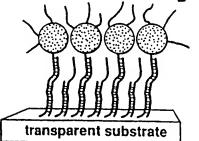




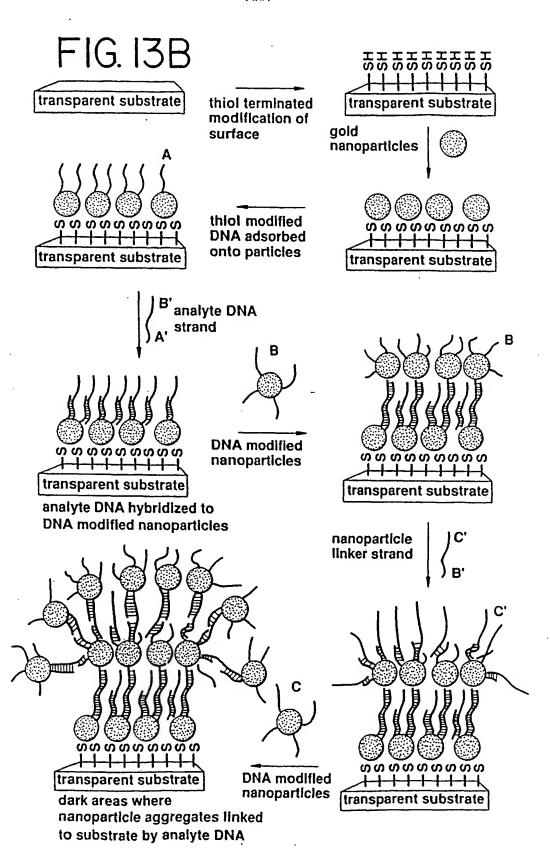


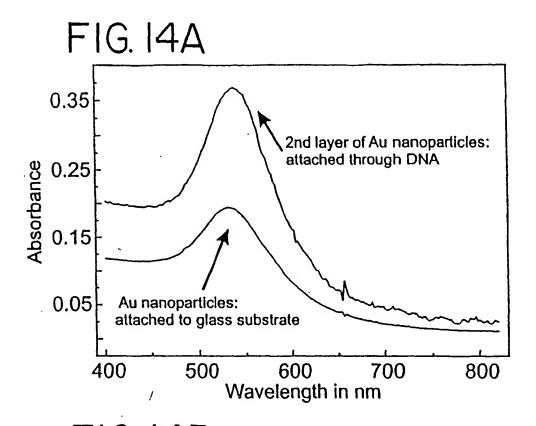
Dark areas where nanoparticle aggregates are linked to substrate surface by analyte DNA

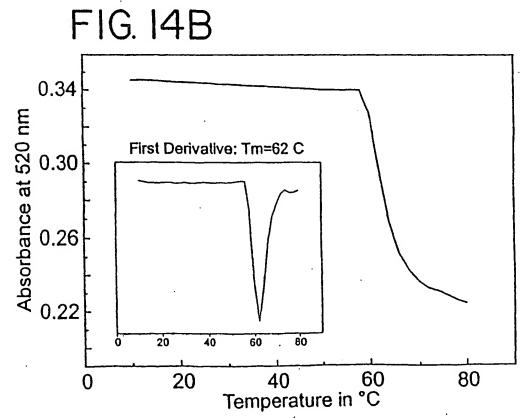


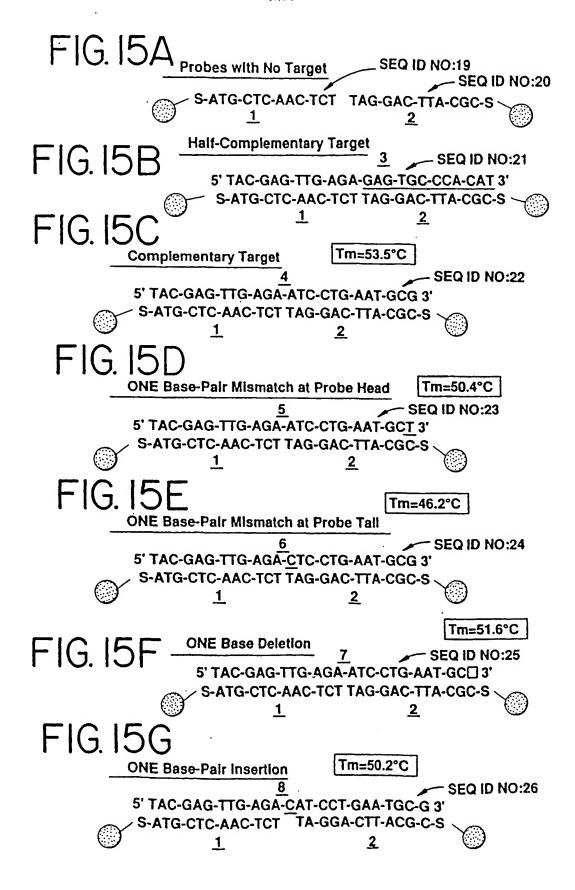


DNA modified colloids hybridized to bound analyte DNA









-16.16A

24 Base Template

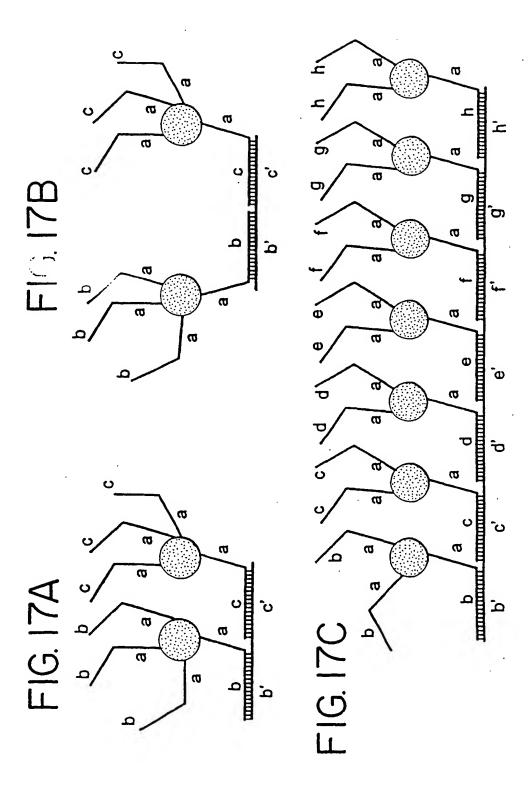
FIG. 16B

48 Base Template with Complementary 24 Base Filler

5' TAC-GAG-TTG-AGA-CCG-TTA-AGA-CGA-GGC-AAT-CAT-GCA-ATC-CTG-AAT-GCG 3' > S-ATG-CTC-AAC-TCT GGC-AAT-TCT-GCT-CCG-TTA-GTA-CGT TAG-GAC-TTA-CGC-S

FIG. 16(

72 Base Template with Complementary 48 Base Filler



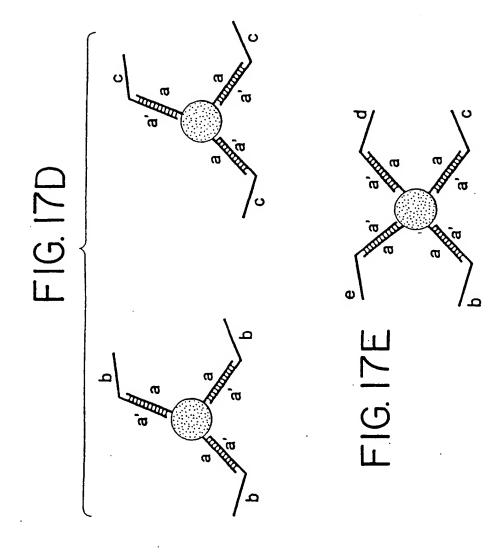
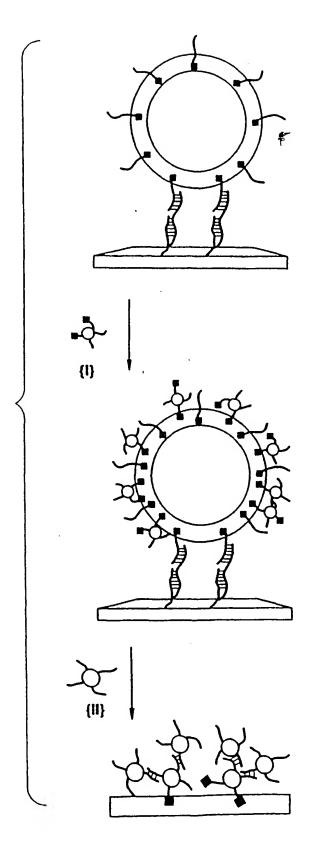


FIG. 18



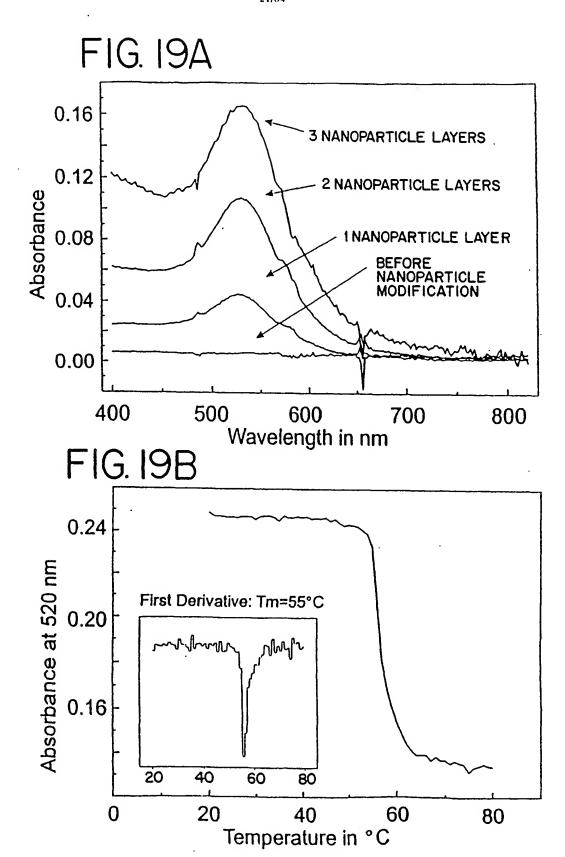
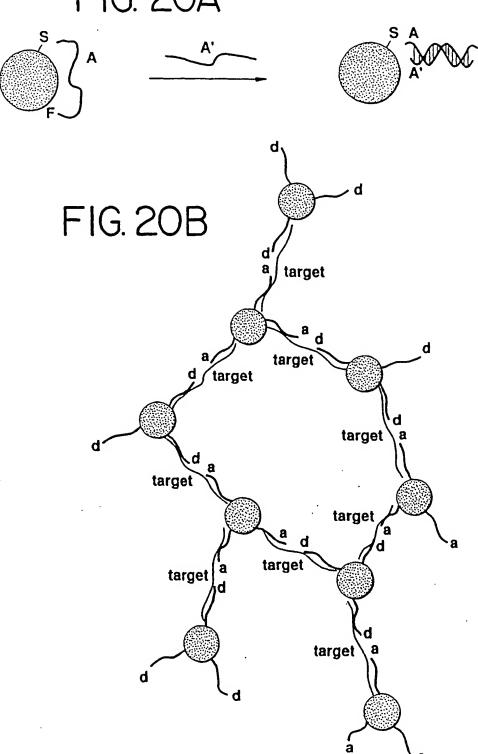


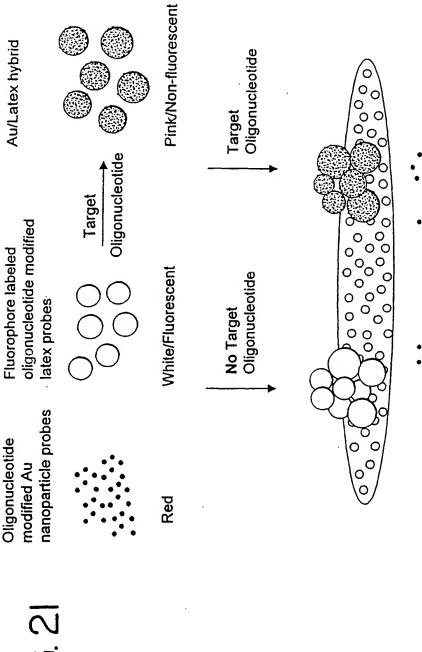
FIG. 20A

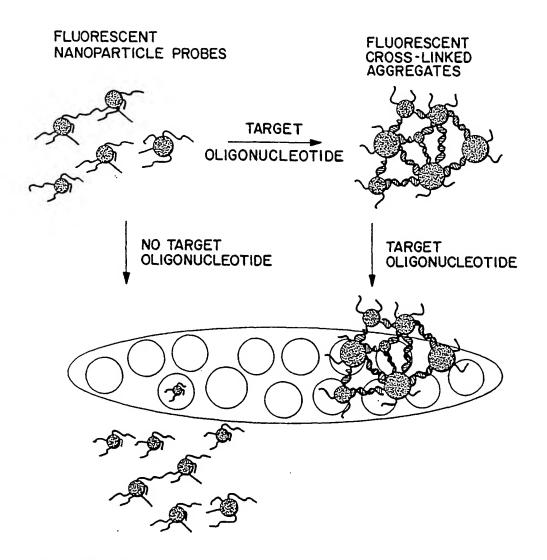


Excess Au probes

pass through membrane

All Au probes pass through membrane





THE FLUORESCENT NANOPARTICLE PROBES PASS THROUGH THE MEMBRANE

THE FLUORESCENT CROSS-LINKED AGGREGATES ARE RETAINED BY THE MEMBRANE

Anthrax PCR Product

5'G GCG GAT GAG TCA GTA GTT AAG GAG GCT CAT AGA GAA GTA ATT AAT 3'C CGC CTA CTC AGT CAT CAA TTC CTC CGA GTA TCT CTT CAT TAA TTA

TCG TCA ACA <u>GAG GGA TTA TTG TTA AAT ATT GAT AAG GAT</u> ATA AGA AAA AGC AGT TGT CTC CCT AAT AAC AAT TTA TAA CTA TTC CTA TAT TCT TTT

ATA TTA TCC AGG GTT ATA TTG TAG AAA TTG AAG ATA CTG AAG GGC TT 3' TAT AAT AGG TCC CAA TAT AAC ATC TTT AAC TTC TAT GAC TTC CCG AA 5'

141 mer Anthrax PCR product [SEQ ID NO:36]

3' CTC CCT AAT AAC AAT

[SEQ ID NO:37]

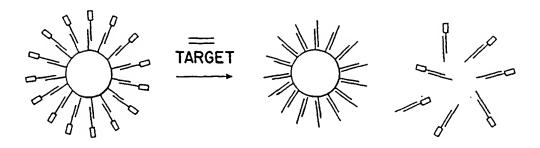
3' TTA TAA CTA TTC CTA

[SEQ ID NO:38]

Oligonucleotide-Nanoparticle Probes

Blocker Oligonucleotides

3' C CGC CTA CTC AGT CAT CAA TTC CTC CGA GT	[SEQ ID NO:39]
3' A TOT OTT CAT TAA TTA AGC AGT TGT	[SEQ ID NO:40]
3' TAT TCT TTT TAT AAT AGG TCC CAA TAT	[SEQ ID NO:41]
3' AAC ATC TTT AAC TTC TAT GAC TTC CCG AA	[SEQ ID NO:42]



SATELLITE PROBE

DETECTION SIGNAL

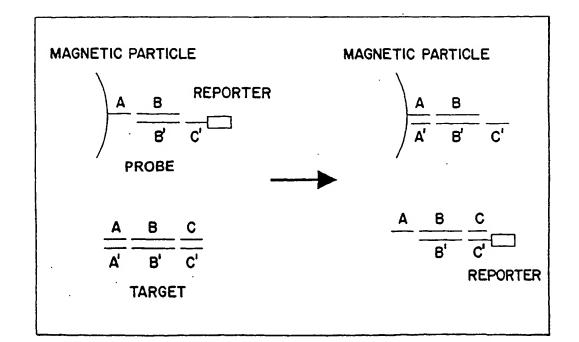
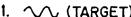
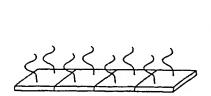


FIG. 25A \sim (target)







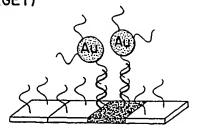
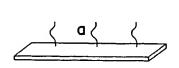
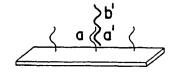
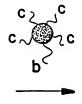


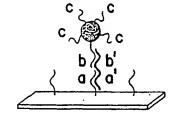
FIG. 25B

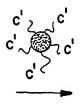


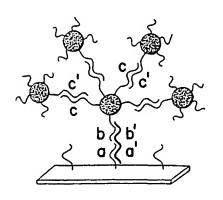














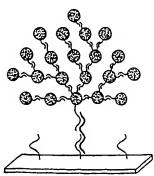


FIG. 26A

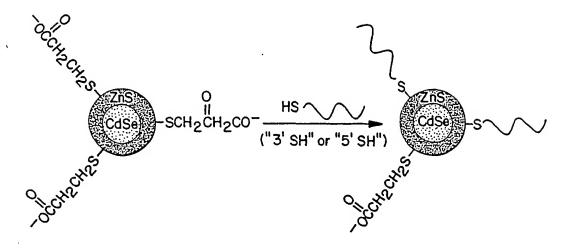
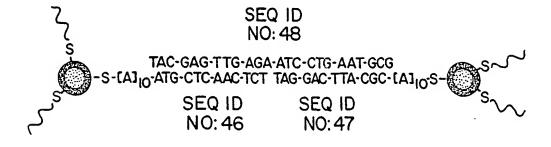


FIG. 26B



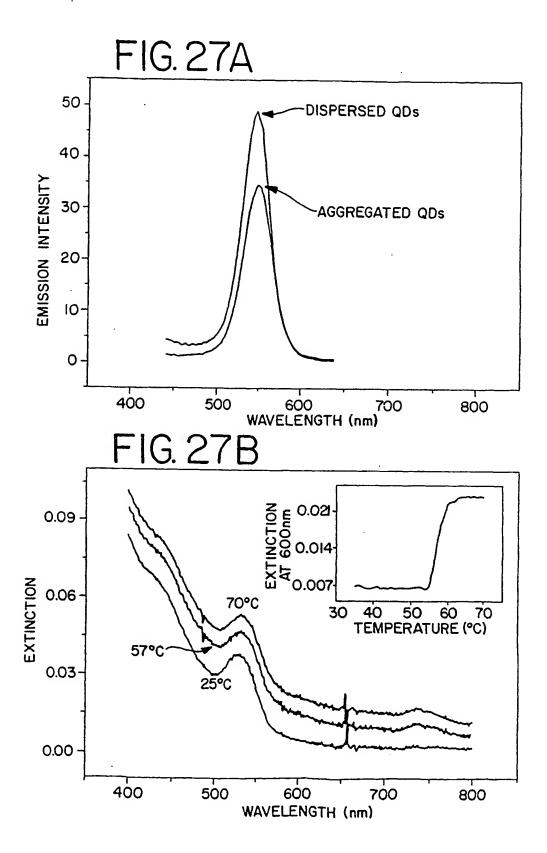


FIG. 27C

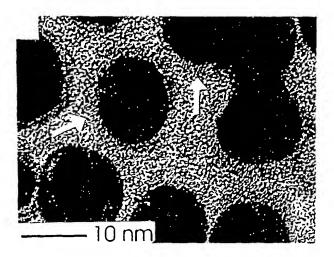


FIG. 27D

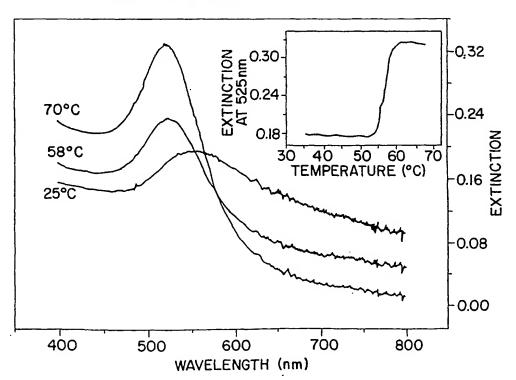


FIG. 28A

FIG. 28B

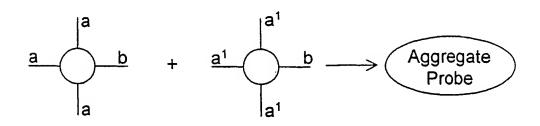


FIG. 28C

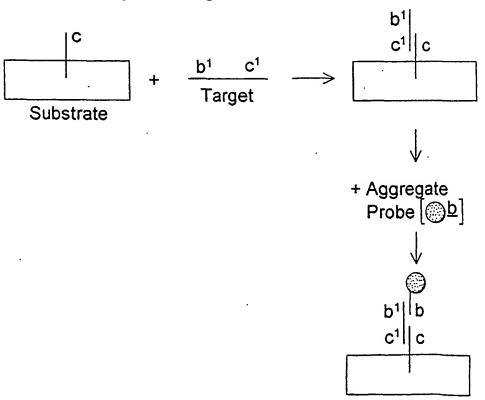


FIG. 28D

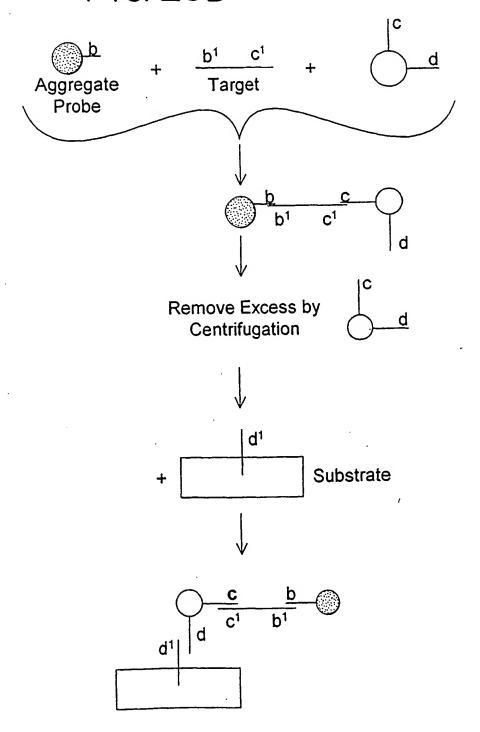
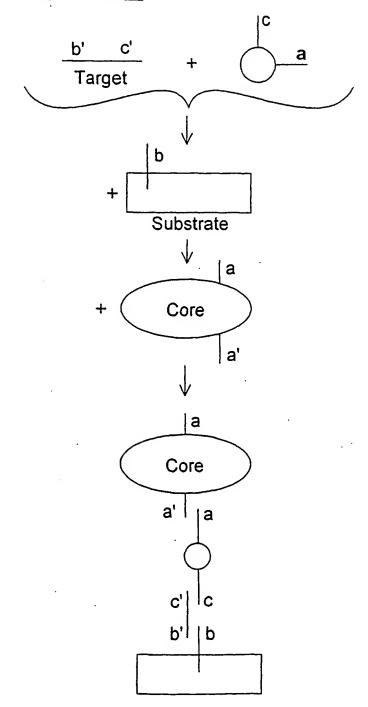
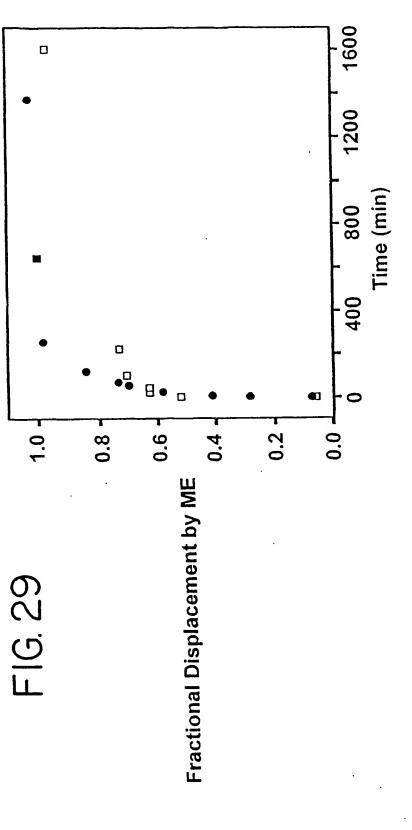
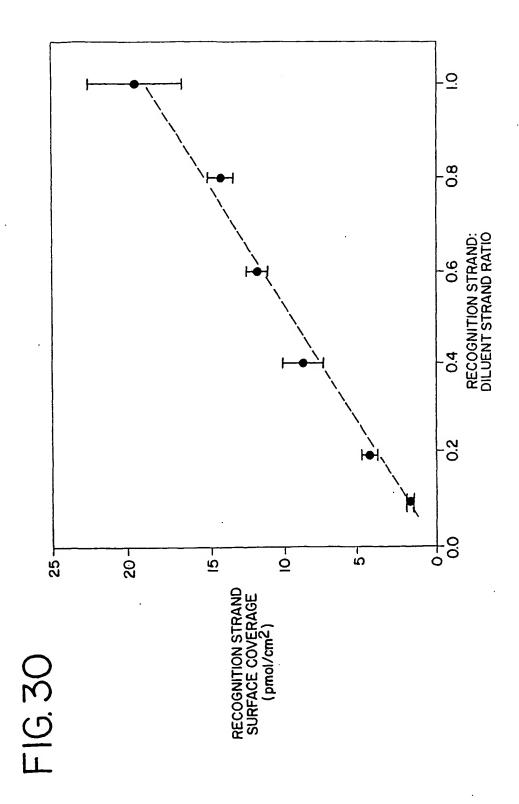


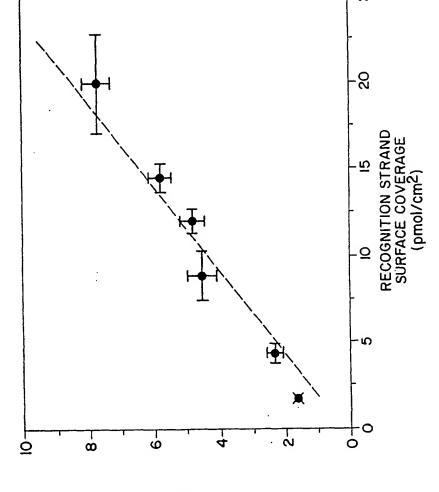
FIG. 28E







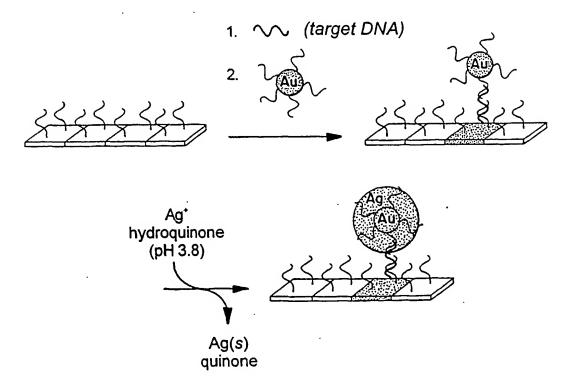


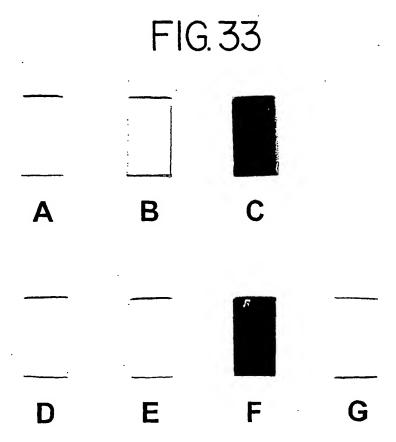


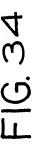
[SEQIDNO:56]

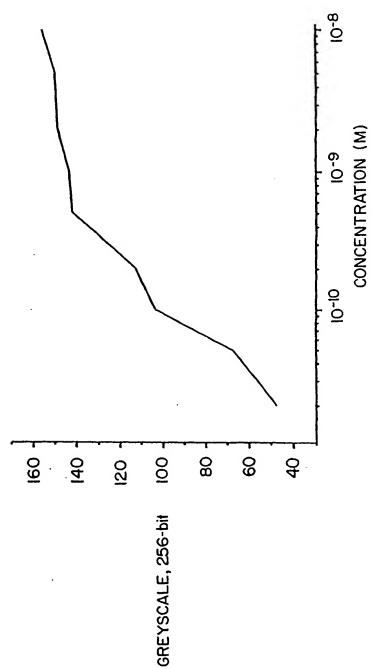
5' GGA T**T**A TTG TTA--AAT ATT GAT AAG GAT 3' CCT A**N**T AAC AAT TTA TAA CTA TTC CTA [SEQ ID NO: 57] [SEQ ID NO: 58]

> **N** = A (complementary), G,C,T (mismatched)











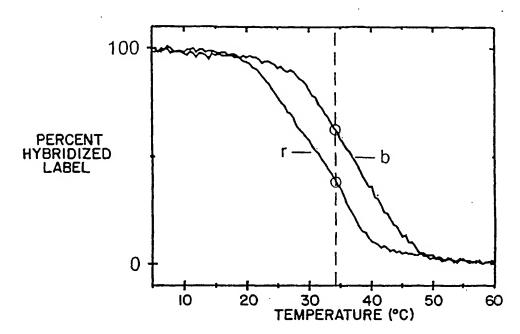


FIG.35B

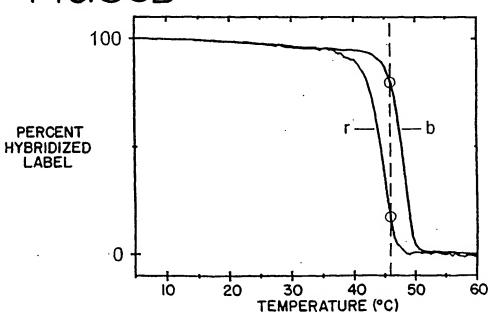


FIG. 36A

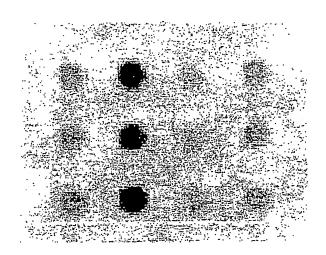
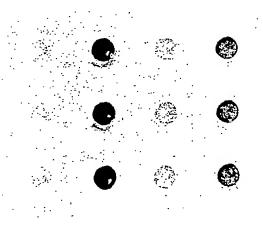


FIG. 36B



 $\mathsf{C}^{\mathsf{L}}\mathsf{A}^{\mathsf{L}}\mathsf{T}^{\mathsf{L}}\mathsf{G}$

FIG.37A

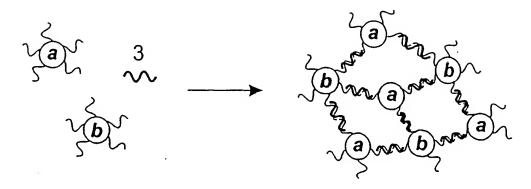
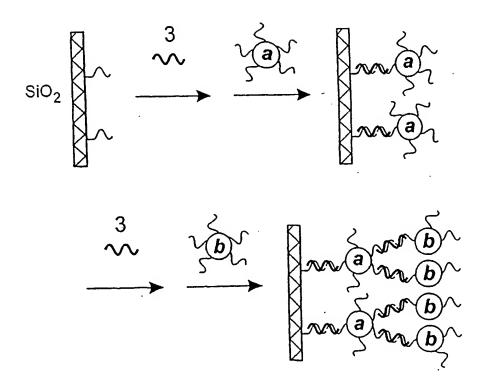
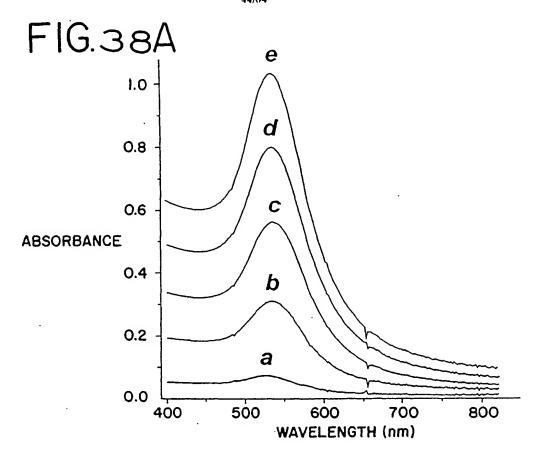


FIG.37B





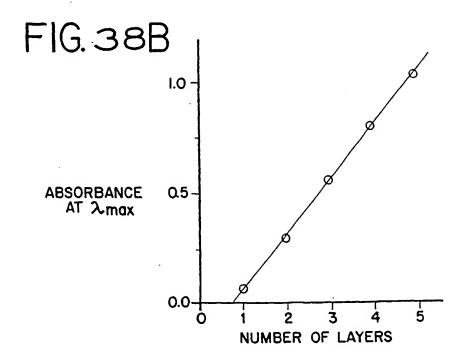


FIG. 39A

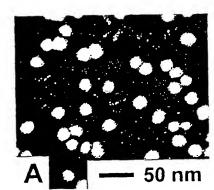
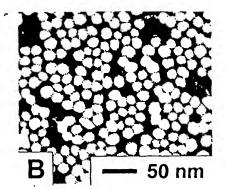
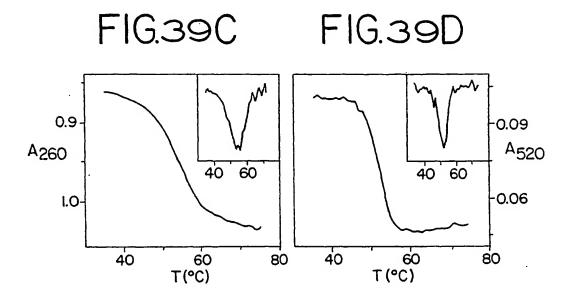
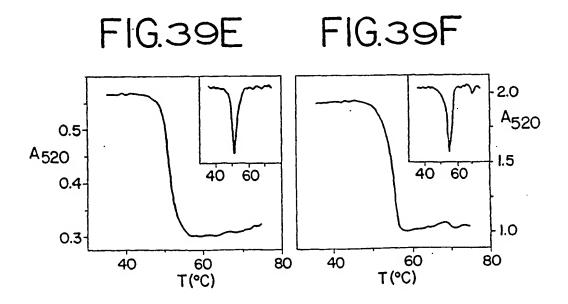
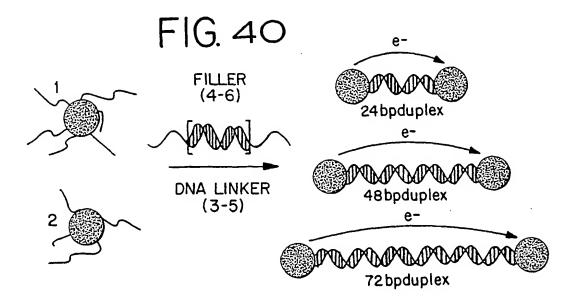


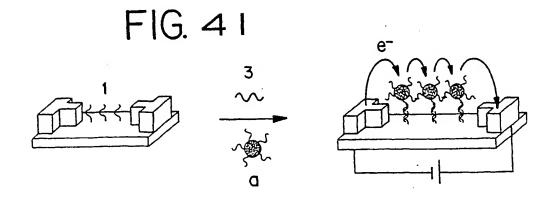
FIG.39B











 R_i

a = H

 $b = (iPr)_2NP(OCH_2CH_2CN)$ -

 $c1 = 5'p(A_{20})$ -TATCGTTCCATCAGCT [SEQ ID NO: 65]

 $c2 = 5'-p(A_{20})$ -TTGATCTTCCGTTCT [SEQ ID NO: 66]

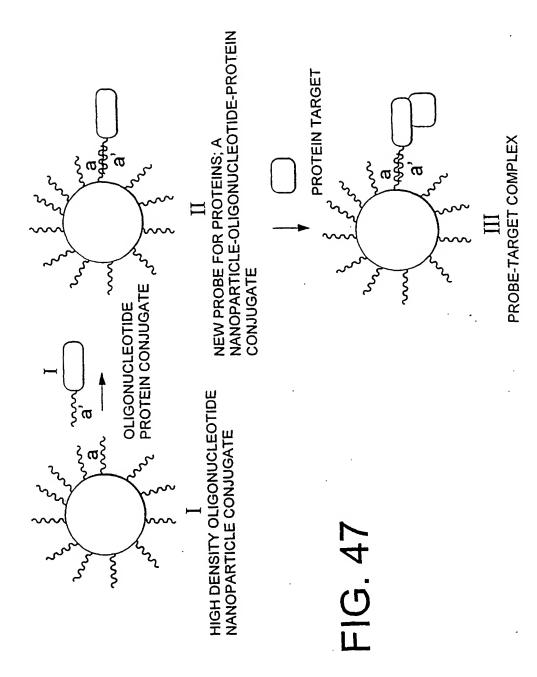
Target I = 79-mer oligonucleotide with target region:

3'-.....ATAGCAAGGTAGTCGAGCAACTAGAAAGGCAAGA.......5'
[SEQ ID NO: 67]

$$R_4$$
-(CH_2)_n R_3 R_4 -NH(CH_2)_n R_3

R₃ = hydrogen, an alkyl group, an aryl group, or a substituted alkyl or aryl group

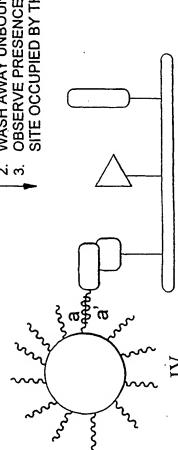
 R_4 = an attached oligonucleotide or modified oligonucleotide



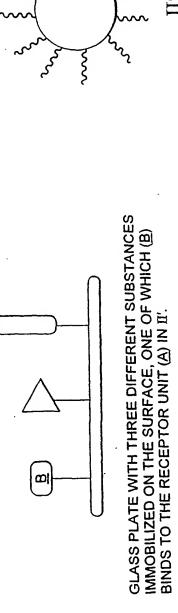
GLASS PLATE WITH THREE DIFFERENT PROTEINS

IMMOBLIZED ON THE SURFACE, ONE OF WHICH
BINDS TO THE PROTEIN IN PROBE II

NEW PROBE FOR PROTEINS; A NANOPARTICLE-OLIGONUCLEOTIDE-PROTEIN CONJUGATE



EXPOSE PLATE TO THE PROBE SOLUTION
 WASH AWAY UNBOUND NANOPARTICLE PROBE
 OBSERVE PRESENCE OF BOUND NANOPARTICLES AT SITE OCCUPIED BY THE FIRST PROTEIN IN THE SERIES.



န္ **ဖ**န္တြ^{*}က

NANOPARTICLE-OLIGONUCLEOTIDE-RECEPTOR

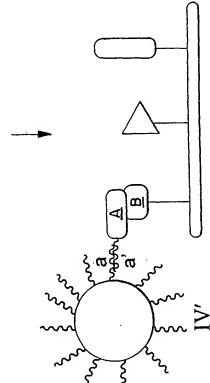
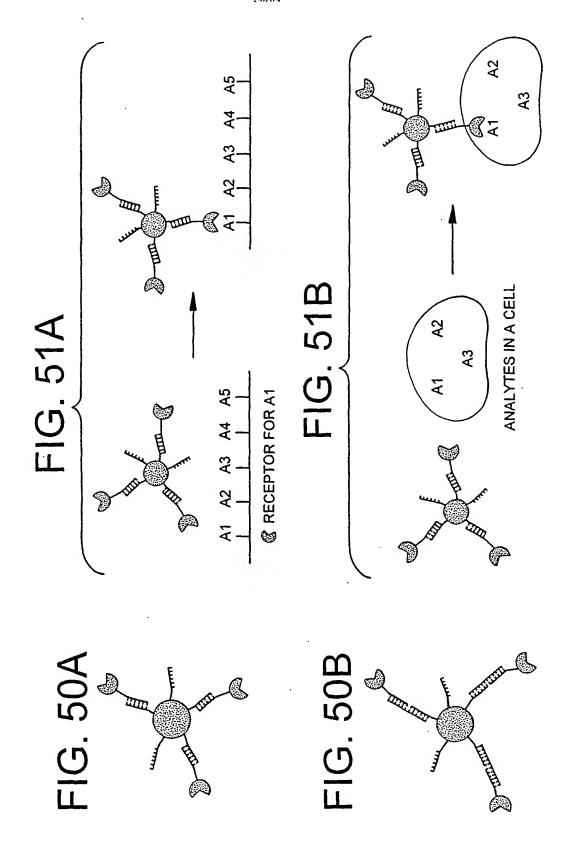
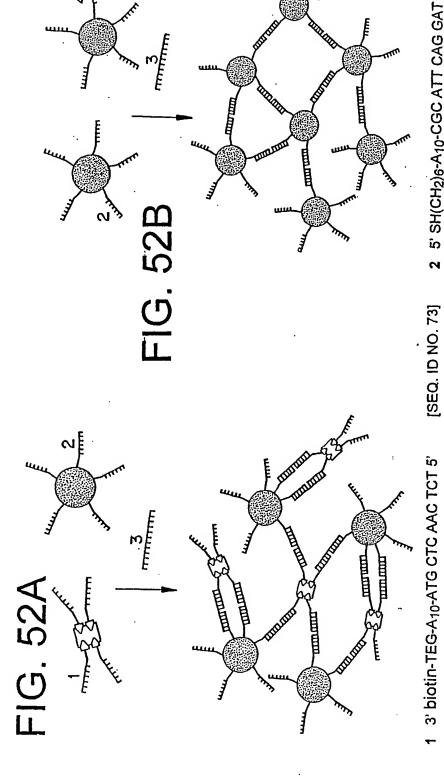


FIG. 49





5' TAC GAG TTG AGA ATC CTG AAT GCG 3' 5' SH(CH₂)6-A₁₀-CGC ATT CAG GAT 3' က

[SEQ. ID NO. 74]

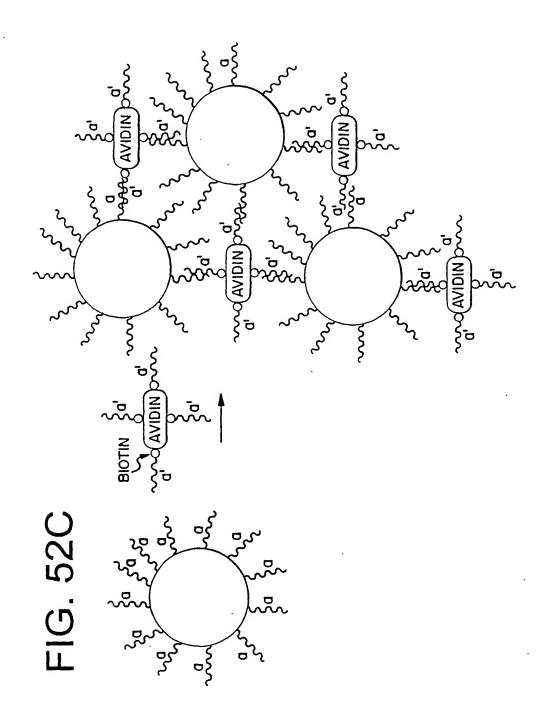
4 3' SH(CH₂)₃-A₁₀-ATG CTC AAC TCT 5'

13 nm AU NANOPARTICLES

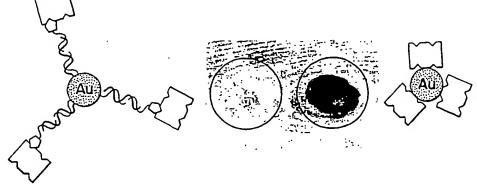
5' TAC GAG TTG AGA ATC CTG' AAT GCG 3' [SEQ. ID NO. 75]

5' SH(CH₂)6-A₁₀-CGC ATT CAG GAT 3'

STREPTAVIDIN (iii) 13 nm Au NANOPARTICLES

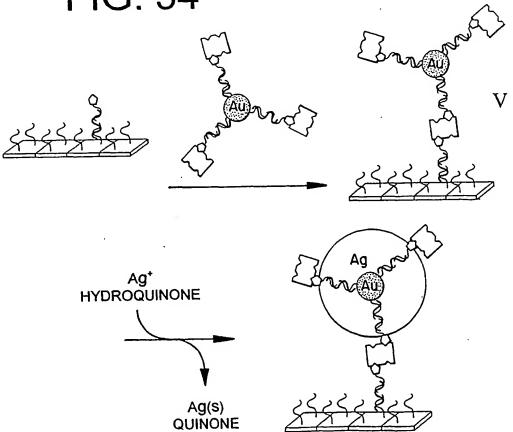


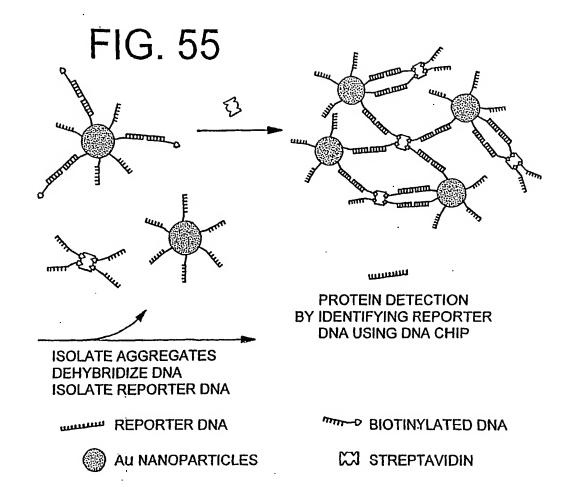




AU COLLOID / DNA / STREPTAVIDIN VS. AU COLLOID / STREPTAVIDIN CONJUGATE CONJUGATE

FIG. 54





1 3' BIOTIN-TEG-A₁₀-ATG CTC AAC TCT 5'

[SEQ.ID NO: 73]

2 5' SH(CH₂)₆-A₁₀-CGC ATT CAG GAT 3'

[SEQ. ID NO: 74]

3 5' TAC GAG TTG AGA ATC CTG AAT GCG 3'

[SEQ. ID NO: 75]



13nm Au NANOPARTICLES



www. LINKER DNA

MINTED DNA

FIG. 57A

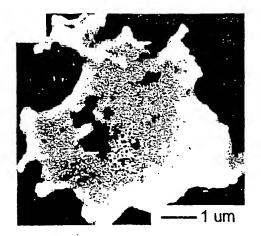


FIG. 57B

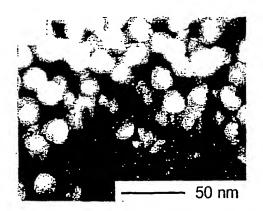


FIG. 58A

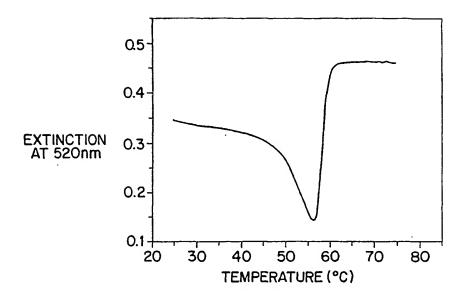


FIG. 58B

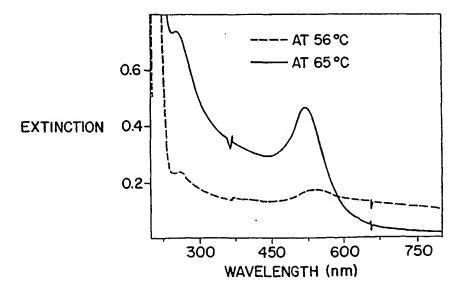


FIG. 59

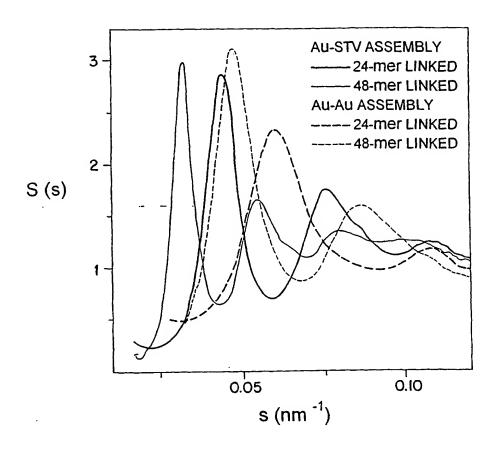
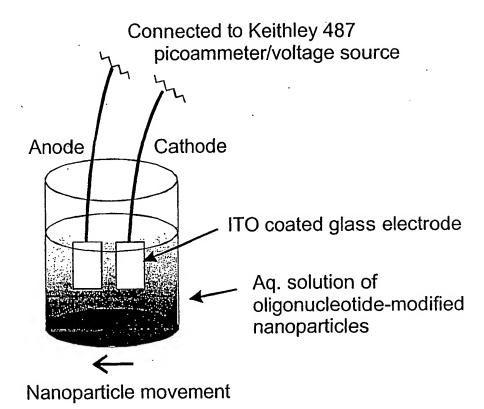


Figure 60

Scheme 1



SEQUENCE LISTING

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 Letsinger, Robert L.
 Mucic, Robert C.
 Storhoff, James J.
 Elghanian, Robert
 Taton, Thomas A.

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<150> PCT/US97/12783

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<150> 09/240,755

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